REMARKS

Claims 1-2, 4-5, 7-14, 16-17, and 19-26 are presently pending. Claims 1, 13, 25, and 26 are the pending independent claims.

Claim 1 has been amended to include the subject matter of claim 3. Support for the amendment can be found throughout the specification at, for example, original claim 3.

The Applicants would like to thank the Examiner for the courtesies extended during the January 11, 2205 telephonic interview and the January 6, 2005 personal interview. The interpretation of the weight ratios in the claims was discussed during the January 11, 2005 interview. Agreement was not reached. The substance of the January 6, 2005 interview is set forth in the Interview Summary. As a result of that interview, new claim 29 has been added. Support for this claim can be found throughout the specification at, for example, paragraph 31.

It is submitted that no new matter has been introduced by the foregoing amendment. Approval and entry of the amendments is respectfully solicited.

Enablement Rejection

Claims 1-2, 4-8, and 11-12 were rejected under 35 USC §112, first paragraph, on the asserted grounds that "the specification, while being enabling for a composition comprising compressible admixture of simethicone and silicified microcrystalline cellulose and magnesium aluminometasilicate, does not reasonably provide enablement for a composition comprising "admixture of simethicone and an absorbent." The Examiner contended that the "specification does not enable any person skilled in the art to which it pertains, to practice the invention commensurate in scope with these claims."

For the reasons set forth below, the rejection is respectfully traversed.

While the rejection is not agreed to, claim 1 has been amended to include the subject matter of claim 3. This amendment was made in view of the Examiner's admission that the specification was "enabling for a composition comprising compressible admixture of simethicone and silicified microcrystalline cellulose and magnesium aluminometasilicate." With this amendment it is believed that the rejection of claim 1 is moot and should be withdrawn.

Because claims 2, 4-8, and 11-12 depend from claim 1, the rejection to these claims is also moot and should be withdrawn.

Indefiniteness Rejection

Claim 2 was rejected under 35 USC §112, second paragraph. (OA at 6.)

For the reasons set forth below, the rejection is respectfully traversed.

In making the rejection, the Examiner asserted that

> Claim 2 recites that the weight ratio of simethicone to adsorbent is "at least about 1:2.00". The scope of the instant claim 2 encompasses "1:1.95, 1:1.96, 1:9.7, 1:9.8, 1:9.9, 1:2.00, 1:2.01, 1:2.02, 1:2.02, 1:2.03, 1:2.04, 1:2.05...1:2.20, 1:2.21...". The scope of the claim 2, for example "1:1.95, 1:1.96, 1:9.7, 1:9.8, 1:9.9, 1:2.00, 1:2.01, 1:2.02, 1:2.03, 1:2.04, 1:2.05", is broader than the scope of the claim 1, "at least about 1:2.22", for example "1:2.20, 1:2.21, 1:2.22, 1:2.23, 1:2.24, 1:2:25, 1:2:26, 1:2.27, 1:2.28, 1:2.29, 1:2.30...". As discussed above, claim 2 fails to further limit the subject matter of the claim 1. This inconsistency leads to lack of clarity of the claims as a whole.

(*Id.*)

The record of the captioned application sets forth ongoing disagreement between the Examiner and the Applicants concerning the proper interpretation of the claims, in particular the claimed weight ratio in claim 2 (as well as claim 1). It does not appear that the guidance provided in the MPEP concerning claim interpretation has been used. The following analysis of the claimed weight ratio in claim 2 is provided in order to clarify the record.

During examination, claims must be given their broadest reasonable interpretation. (MPEP § 2111.) The words of a claim must be given their plain meaning, which refers to the ordinary and customary meaning given to the term by those of ordinary skill in the art, unless they are defined in the specification. (MPEP § 2111.01) The ordinary and customary meaning of a term may be evidenced by a variety of sources, including the claims themselves, dictionaries and treatises, and the written description, the drawings, and the prosecution history. (*Id.*) It is appropriate to compare the meaning

of terms given in technical dictionaries in order to ascertain the accepted meaning of a term in the art. (MPEP § 2173.05(b)III.)

It is respectively submitted that the interpretation of the claimed weight ratio relied on by the Examiner is contrary to the ordinary and customary meaning of the term "ratio." In view of MPEP § 2173.05(b)III concerning the appropriateness of comparing the meaning of a term in technical dictionaries, attached hereto is a copy of the definition of the term "ratio" from two different technical dictionaries, which were published before the filing date of the captioned application. Specifically these are:

1) Academic Press Dictionary of Science and Technology (1992)

> RATIO is "a statement of the relative size of two quantities (numbers, functions, and so on) expressed as a quotient. The ratio of A to B is written as A/B or A:B.

2) Larousse Dictionary of Science and Technology (1995).

> RATIO is "the ratio a:b is equivalent to the quotient a/b."

Thus, the term "ratio" is a quotient A/B or A:B. The definition for the term quotient in the two technical dictionaries relied on above is also attached hereto. As seen therein, a quotient is, among other things, "the result of performing the arithmetic operation of division" or, in other words, the result of the operation of determining how many times one number, the divisor (denominator), is contained in a second, the dividend (numerator).

Under the ordinary and customary meaning objectively provided by the technical dictionaries set forth above, the interpretation of the claimed weight ratio in Claim 2 of "at least about 1:2.22" is properly interpreted as "at least the quotient 1:2.22," which is equivalent to the quotient 1/2.22.

The Applicants attempted to aid the Examiner in interpreting the claimed weight ratios by expressing them as a quotient in the January 21, 2003 Amendment ("the captioned application [was] amended to expressly provide the quotient of the ratio").. However, the Examiner objected to such amendments under 35 USC § 132 as allegedly containing new matter. (Paper No. 9 at 3.) While the Examiner's position was disagreed with, the quotients were cancelled in August 29, 2003 Response, Including Amendment. The Examiner continues, however, to maintain the rejection based upon an interpretation of the claims that appears to be contrary to the plain meaning of the team.

Not only is the Applicants' position supported by technical dictionaries, the written description, including the examples contained therein also support their position. MPEP § 2111.01 states that "the ordinary and customary meaning of a term may be evidenced by a variety of sources, including the claims themselves, dictionaries and treatises, and the written description, the drawings, and the prosecution history" (emphasis added.) For instance, Examples 1-3 and 5-11 support the interpretation advocated by the Applicants in view of claims 1 and 2. In addition, the weight ratios listed in paragraph 32 are ordered from broad to narrow. Therefore, it is respectfully submitted that the plain meaning of claim 2 is clear. The rejection is improper and should be withdrawn.

Anticipation Rejection

Claims 1-2 and 4-5 were rejected under 35 USC §102(b) as anticipated by Stevens, US Patent No. 5,679,376, ("Stevens"). (OA at 5.)

For the reasons set forth below, the rejection, respectfully is traversed.

Stevens discloses

A solid oral dosage form for the treatment of gastrointestinal disorders comprising a therapeutically effective amount of a pharmaceutical suitable for the treatment of gastric disorders selected from the group consisting of cimetidine, ranitidine, famotidine, diphenoxylate, loperamide, loperamide-N-oxide, pharmaceutically acceptable salts thereof and combinations thereof; and a therapeutically effective amount of simethicone wherein the pharmaceutical and simethicone

(Abstract)

FIG. 6 provides dissolution profiles for three formulations of uncoated loperamide present with simethicone provided in an admixed single solid oral dosage form. The solid line indicates the dissolution profile of loperamide from a solid dosage form comprised of Simethicone GS-J (40% simethicone adsorbed onto a diluent) and uncoated granules containing loperamide. The dashed line indicates the dissolution profile of loperamide from a second solid dosage form containing granules of Simethicone GS-J (40% simethicone adsorbed onto a diluent) and uncoated granules containing loperamide. The dotted line indicates the dissolution profile of loperamide from a third solid dosage form containing granules of Simethicone GS-J (40% simethicone adsorbed onto a diluent) and uncoated granules containing loperamide. The formulations for these solid dosage forms are contained in Example I.

(Col. 2, lns. 40-55.)

The simethicone used in the present invention can be Simethicone USP or a commercially prepared granulation such as Simethicone GS (30% Simethicone USP adsorbed onto maltodextrins available from Union Carbide) or Simethicone GS-J (40% Simethicone USP adsorbed onto maltodextrins available from Union Carbide). The amount of simethicone contained in the solid dosage form should be sufficient to provide a therapeutic dosage to a patient suffering from gas or diarrhea and its associated symptoms. The preferred dosage ranges for simethicone is in the range of about 20 mg to about 125 mg per dosage unit, generally not to exceed 500 mg/day. The dosage ranges may vary for age and weight of a patient as well as the severity of symptoms. (Col. 4, lns. 31-43.)

Ingredient	Mg/Tablet
Simethicone, USP	125.0
Dibasic Calcium Phosphate, USP	370.0
Microcrystalline Cellulose, NF	265.5
Colloidal Silicon Dioxide, NF	31.5
Sodium Starch Glycolate, NF	72.0
Croscarmellose Sodium, NF	36.0
Loperamide HCl, USP	2.0
Total	902.0

DIRECTIONS: .

The third experimental tablet was manufactured in the following manner:

1. Mix loperamide HCl, dibasic calcium phosphate and microcrystalline cellulose in a planetary mixer (Hobart mixer) for 30 seconds.
2. Granulate by adding simethicone into Step 1 for 1 minute.
3. While mixing add colloidal silicon dioxide to Step 2 for 2.5 minutes.
4. Add sodium starch glycolate and croscarmellose sodium and mix for 1 minute.
5. Compress the tablets as set forth above for the first experimental tablet.

FIG. 5 shows the dissolution profile of simethicone and loperamide when provided in separate solid oral dosage form. As is shown in FIG. 6, the dissolution profile of loperamide in tablets containing both loperamide and simethicone in a single solid oral dosage form was reduced to the point that almost no loperamide was detected. The solid, dashed and dotted lines in FIG. 6 represent the dissolution profiles for the first, second and third experimental tablets, respectively. These results demonstrate the need for a new solid oral dosage form containing a combination of simethicone and a pharmaceutical suitable for the treatment of a gastric disorders.

In making the rejection, the Examiner merely stated that "[t]his rejection is analogous to the original rejection." (Paper No. 9 at 5.) In the original rejection, the Examiner contended only that "Stevens teaches a solid oral dosage form comprising loperamide, simethicone, microcrystalline cellulose and colloidal silicone dioxide,

wherein a ratio of simethicone and microcrystalline cellulose is about 1.2.12 (125 mg :265.5 mg) or a ratio of simethicone and a combination of colloidal silicon dioxide and microcrystalline cellulose is about 1:2.37 (125 mg:297 mg). (Paper No. 5 at 5.) The Examiner appears to have taken official notice that the use of microcrystalline cellulose and colloidal silicon dioxide were inherently adsorbents. Further, the Examiner concluded that since the calculated ratio of 1:2.12 (simethicone to microcrystalline cellulose) or 1 2.37 (simethicone to the combination of microcrystalline cellulose and colloidal silicon dioxide) fell within the claimed ration of simethicone to adsorbent of at least about 1:2.22 (claim 1) and at least 1:2. (*Id.*)

As is well settled, anticipation requires "identity of invention." Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim.

We note that the claim 1 been amended. It is respectfully submitted that the rejection of claim 1 is moot. Therefore, the rejection should be withdrawn.

Because claims 2, 4, and 5 depend from claim 1, the rejection to these claims based on Stevens is also moot and should be withdrawn.

Claims 1-2, 4-5. 7-8, and 11-12 were rejected under 35 USC §102(b) as anticipated by Luber et al., US Patent No. 6,103,260, ("Luber"). (OA at 6.)

For the reasons set forth below, the rejection respectfully is traversed.

Luber discloses

> In accordance with the present invention, the simethicone is admixed with the granulated anhydrous tribasic or dibasic calcium phosphate to form a uniform free flowing granular composition. Generally, it is desired that the admixture contain a proportionate amount of the simethicone antifoam agent and granular anhydrous calcium phosphate which is consistent with forming a free-flowing granular composition. Preferably, the proportionate amounts of the ingredients of the granular admixture composition is about 10–70% w/w simethicone and about 30–90% w/w granular anhydrous tribasic or dibasic calcium phosphate. The ingredients (Col. 3, lns. 31-41.)

Optionally, the dosage form can include one or more additional active ingredients suitable for the treatment of gastrointestinal disorders, for example heartburn, ulcers or diarrhea. Suitable active agents for treating gastrointestinal disorders include heartburn or antiulcer medicaments such as sucralfate, the H2 receptor antagonists cimetidine, ranitidine, famotidine or nizatidine, proton pump inhibitors such as omeprazole or lansoprazole; antidiarrheal agents such as loperamide and diphenoxylate; gastrointestinal motility agents such as cisapride, and antacids such as aluminum hydroxide, magnesium carbonate, magnesium hydroxide, calcium carbonate and the like. The amount of such additional active ingredient combined with the simethicone should be an amount sufficient to provide a therapeutic dosage to a patient suffering from the gastrointestinal disorder being treated. (Col. 5, lns. 13-28.)

EXAMPLE 1

Preparation of Simethicone/Granular Anhydrous Tribasic Calcium Phosphate Admixture

1. 700 gm of granular tricalcium phosphate (Tritab®, Rhone-Poulenc, Shelton, Conn.) is added to the mixing bowl of a Kitchen Aid mixer.
2. While mixing at low speed, over a period of 5 minutes add 200 gm of simethicone, USP.
3. Continue mixing at low speed for an additional 5 minutes.
4. Add 2.5 gm of silicon dioxide and mix an additional 5 minutes.

This intermediate is a free flowing granulation with no large agglomerates. (Col. 5, lns. 31-44.)

EXAMPLE 2

Preparation of Simethicone/Granular Anhydrous Dibasic Calcium Phosphate Admixture

1) 700 gm of granular anhydrous dibasic calcium phosphate, (Emcompress® Anhydrous, Mendell, Paterson, N.J.) is added to the mixing bowl of a Kitchen Aid mixer.
2) While mixing a low speed, over a period of 5 minutes add 200 gm of simethicone, USP.
3) Continue mixing at low speed for an additional 5 minutes.
4) Add 7.5 gm of silicon dioxide and mix an additional 5 minutes.

This intermediate is a free flowing granulation with no large agglomerates.

(Col. 5, lns. 45-59.)

EXAMPLE 4

Preparation of Chewable Tablets Containing Simethicone/Granular Anhydrous Tribasic Calcium Phosphate Admixture

1) 1500 gm of tricalcium phosphate powder was dry granulated by roller compacting at a roll pressure of 500 psi.
2) The compact was passed through a Fitz Mill with a 0.093" screen, knives forward.
3) The milled material was screened, and the -30 to +80 mesh fraction collected as product.
4) 700 gm of compacted tricalcium phosphate granules was added to the mixing bowl of a Kitchen Aid mixer.
5) While mixing a low speed, over a period of 5 minutes add 200 gm of simethicone, USP.
6) Continue mixing at low speed for an additional 5 minutes.
7) Add 20 gm of tricalcium phosphate powder and mix an additional 5 minutes.

This intermediate is a free flowing granulation with no large agglomerates.

8) 91 gm of the above intermediate was then blended with 98 gm of Dextrates, 7.5 gm granular sorbitol, 0.6 gm peppermint flavor, and 0.5 gm stearic acid.
9) The blend was finally compressed using ⅝" FFBE tooling. The tablet weight was 1300 mg. The physical properties of the tablet were:

   Hardness: 11–12 kp

   Friability: less than 0.1% at 100 drops

   Disintegration in N/10 HCl: less than 1.5 minute

   Defoam: 7 secs

(Col. 6, lns 28-58.)

EXAMPLE 6

Preparation of Swallowable Film Coated Tablets Containing Simethicone/Granular Anhydrous Tribasic Calcium Phosphate Admixture

Ingredient	Qty mg/tab
PART I - concentrate	
Tribasic calcium phosphate, NF, Anhydrous, granular	500
Simethicone, USP	25
Tribasic calcium phosphate, NF, Anhydrous, Powder	25
PART II- Scavenger	
Tribasic calcium phosphate, NF, Anhydrous, Powder	20
PART III- Excipient/Binder system	
Dibasic calcium phosphate, Dihydrate, USP	105.75
Microcrystalline cellulose, NF (MCC)	50
Crystalline sorbitol, NF	70
Croscarmellose sodium, NF	30
PART IV-Lubricant	
Magnesium Stearate, NF	0.5

PART 1) A concentrate comprised of granular and powdered anhydrous tribasic calcium phosphates, and simethicone is prepared by adding simethicone compound, USP to a moving bed of granular tribasic calcium phosphate so that the simethicone is distributed evenly and the granular calcium phosphate particle size remains essentially unchanged. The bed is kept in motion by low shear mixers such as fluid bed, Nauta, PK without intensifier bar, pin mixer, or ribbon mixer. After the bed has adsorbed the simethicone, anhydrous tribasic calcium phosphate powder is added. The granulation may then be screened through a No. 20 US Std screen (~840 micron).

PART 2) When a final blend for compression is desired an additional quantity of calcium phosphate powder is added to the PART 1 concentrate and blended.

PART 3) Excipients including a disintegrant are then added with low shear blending which imparts uniform distribution of the active within a binding matrix of limited compositional range.
PART 4) The final addition step is to add a lubricant.
PART 5) The blend is compressed into tablets using a rotary tablet press.
PART 6) Tablets are then film coated and/or gelatin dipped.
Typical film coated tablet characteristics:
Hardness range: 6–14 kp
Tablet weight (core): Approx. 1000 mg
USP disintegration time in water : Less than 7 minutes, in acid media : Less than 6 minutes
USP Defoaming activity time: 9 seconds (Col. 7, line 26 – col. 8, line 13.)

In making the rejection of claims 1-2 the Examiner asserted that "Luber teaches an antifoam oral solid dosage form preparations formed from a free [f]lowing granular composition comprising an admixture of simethicone and [] either one or both of granular anhydrous tribasic calcium phosphate or dibasic calcium phosphate, wherein the simethicone is adsorbed by the granular anhydrous tribasic or dibasic calcium phosphate or mixture thereof, and where ratios of simethicone to granular tricalcium phosphate are 1:3/.5 in Examples 1-2 and 1:4 in Example 6. (OA at 6.) The Examiner further asserted "[a]lthough Luber is silent about the use of granular tribasic calcium phosphate or dibasic calcium phosphate as an adsorbent" such compounds "read[] on the broadly defined term "adsorbent." Based upon this, the Examiner concluded that "the reference clearly anticipates the claimed invention" because "the claimed weight ratio of simethicone to adsorbent" encompasses the weight ratio of simethicone to tribasic calcium phosphate or dibasic calcium phosphate disclosed in Luber.

As is well settled, anticipation requires "identity of invention." Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim.

We note that the claim 1 been amended. It is respectfully submitted that the rejection of claim 1 is moot. Therefore, the rejection should be withdrawn.

Because claims 2, 4-5. 7-8, and 11-12 depend from claim 1, the rejection to these claims based on Luber is also improper and should be withdrawn.

Obviousness Rejection

Claims 3, 9-10, 13-15, and 19-26 were rejected under 35 USC §103(a) as being unpatentable over Kitsusho Yakuhin Kogyo KK (JP 398241) ("Kitsusho") in view of Tobyn et al, (International Journal of Pharmaceutics 169 (1998) 183-194) ("Tobyn") (OA at 9.)

For the reasons set forth below the rejection, respectfully is traversed.

Kitsusho discloses discloses a method for preparing simethicone tablets by mixing and granulating simethicone with aluminum silicate, magnesium aluminum metasilicate, and magnesium silicate. (p. 2.) In particular, the formulation disclosed by the above Japanese patent requires at most 25 % simethicone and 75% or greater silicate, binder and dispersing agent. Binders were disclosed as being starch and lactose. Dispersing agent was disclosed as being carboxymethylcellulose. Further, Kitsusho discloses that when the amount of simethicone exceeds 25%, a portion of the simethicone can be carried away, therefore the tablet workability is not desirable.

Tobyn discloses a comparison between microcrystalline cellulose ("MCC") and silicified microcrystalline cellulose ("siMCC"). According to Tobyn, MCC has properties such as low bulk density, high lubricant sensitivity, poor flow characteristics, and influence of moisture on the compression characteristics. (Tobyn at 183.) Tobyn disclosed that surface treatment of MCC with silicon dioxide or silicic acid had beneficial characteristics with respect to disintegration and mechanical resistance. (Tobin at 184.) Tobyn also discloses that siMCC was chosen to possess a number of pharmaceutical advantages in terms of powder flow, tablet strength, lubricant sensitivity and we granulation. (Tobyn at 184.) Tobyn disclosed making a dry mix using Emcocel 90 M and dried silica and a wet mix was made using Emcocel 90 M with colloidal silica dispersion, which was tray dried and milled. (Tobyn at 184-85.) Tobyn concluded that no bulk chemical changes in MCC occurred with converted to siMCC. (Tobyn at 193.) Tobyn went on to postulate that "[t]he fundamental chemical properties of the novel material are very similar to the parent material." (Tobyn at 193.) Tobyn also disclosed that siMCC had improved functionality in terms of improved bulk physical properties and mechanical characteristics due to some other intrinsic property rather than a change in the base chemical parameters of the novel material. (*Id.*)

In making the rejection, the Examiner asserted that Kitsusho teaches "teaches a method for preparing simethicone tablets by mixing and granulating simethicone with magnesium aluminum metasilicate. (OA at 12.) The Examiner further asserted that the "formulation disclosed by Kitsusho requires at most 25% simethicone and 75% or greater silicate, binder (i.e., starch and lactose) and dispersing agents (i.e., carboxymethylcellulose)." The Examiner also contended that " [Kitsusho] teaches that when the amount of simethicone exceeds 25% there is a tendency that a portion of the simethicone can be carried away, therefore the tablet workability is not desirable." (OA at 10.) The Examiner acknowledged, however, that Kitsusho differs from the presently claimed invention in that:

1. the incorporation of silicified microcrystalline cellulose in said composition;
2. at least 30 wt% simethicone in said composition;
3. the specific amounts of silicified microcrystalline cellulose and magnesium aluminometasilicates in said composition; and
4. the specific har[d]ness of value of the tablet. (OA at 10.)

To fill the acknowledged gap, the Examiner relied upon Tobyn as disclosing the advantage of using silicified microcrystalline cellulose in improving tablet workability such as "powder flow," "tablet strength," "lubricant sensitivity" and "wet granulation." (*Id.* at 12.)

The Examiner then concluded that "[t]o incorporate such teaching into the teaching of Kitsusho, would have been obvious in view of Tobyn, who teaches the advantage of using silicified microcrystalline cellulose as a pharmaceutical excipient [] to improve powder flow characteristics, lubricant sensitivity, tablet strength and better bulk physical properties. (*Id*). The Examiner reasoned that that "[o]ne having ordinary skill in the art would have been motivated, with a reasonable expectation of success, to incorporate silicified microcrystalline cellulose having good free-flowing and disintegrating properties (which is relatively new pharmaceutical excipients in the art) such that the table workability would be significantly improved. (*Id.*) The Examiner reasoned further "one having ordinary skill in the art would have been motivated to

increase the amount of simethicone above 25% in the solid final blend for tableting by incorporating silicified microcrystalline cellulose in said composition." (OA at 10-11.)

The Examiner then asserted that "[a]lthough the prior art references are silent about the specific dosage amounts of active ingredients and the hardness value of tablet, the optimization of [known] active and inactive ingredients in a composition or the determination of optimum hardness value of the tablet is well considered within the skill of the artisan, absent evidence to the contrary."

Obviousness, cannot be based upon speculation. Nor can obviousness be based upon possibilities or probabilities. Obviousness ***must*** be based upon facts, "cold hard facts." When a conclusion of obviousness is not based upon facts, it cannot stand.

"Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

The rejection uses Tobyn to fill in the acknowledged gaps in Kitsusho, yet fails to point out where in Tobyn even one experiment using simethicone is disclosed. The rejection then summarily concludes that one having ordinary skill in the art would have been motivated to increase the amount of simethicone above 25% in the solid final blend for tableting by incorporating silicified microcrystalline cellulose in said composition.

However, the record does not support such a conclusion. It is not seen where Examiner provided any facts in Tobyn to indicate that simethicone, a viscous oil-like substance, **could be adsorbed onto silicified microcrystalline cellulose**. Nor is it seen

where any facts in this record support such an assertion. Thus, the rejection is not supported by fact and must be withdrawn for this reason alone.

Further, the Examiner has not provided any facts to support the proposition that using siMCC in Kitsusho's formulation would overcome the problem acknowledged by Kitsusho, e.g., not exceeding 25% simethicone in the formulation. It is not seen where there are any facts in the rejection to suggest any expectation of success for increasing the amount of simethicone in a formulation using adsorbents including siMCC and aluminometasilicate. Because it appears that the rejection is based upon possibilities or probabilities, it is improper and should be withdrawn.

Nor is it seen where the record contains any facts indicating that silicified microcrystalline cellulose in combination with aluminometasilicate in any amount could be formulated with simethicone. For this additional reason, the rejection is improper and should be withdrawn.

Claims 16 and 17 were rejected under 35 USC §103(a) as being unpatentable over Kitsusho in view of Tobyn and Stevens. (OA at 11.)

For the reasons set forth below the rejection, respectfully is traversed.

The disclosures of Kitsusho, Tobyn, and Stevens set forth above are herein incorporated by reference.

In making the rejection, the Examiner asserted that "the modified teaching of Kitsusho includes all that is recited in claims 16 and 17 except for the incorporation of active pharmaceuticals such as famotidine. (OA at 13.) To fill the acknowledged gap, the Examiner relied on Stevens as "teach[ing] or suggest[ing] the use of simethicone and other pharmaceutical excipients in preparing oral solid dosage form containing H2 blockers (e.g.., famotidine). (OA at 13.)

The Examiner contended that "[o]ne having ordinary skill in the art would have known that simethicone is routinely combined with H2 blockers (e.g., famotidine) in solid oral dosage formulation art, and would have been further motivated to further modify the teaching of Kitshusho such that the better solid dosage form containing famotidine would be formulated. (OA at 13-14.) The Examiner reasoned "[o]ne having ordinary skill in the art would have been motivated to do this so that the tablet workability would be significantly improved." (OA at 14.)

Obviousness, cannot be based upon speculation. Nor can obviousness be based upon possibilities or probabilities. Obviousness ***must*** be based upon facts, "cold hard facts." When a conclusion of obviousness is not based upon facts, it cannot stand.

"Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

The rejection uses Tobyn to fill in the acknowledged gaps in Kitsusho, yet fails to point out where in Tobyn discloses simethicone, much less even one experiment using simethicone is disclosed. The rejection then summarily concludes that one having ordinary skill in the art would have been motivated to increase the amount of simethicone above 25% in the solid final blend for tableting by incorporating silicified microcrystalline cellulose in said composition.

However, the rejection does not support such a conclusion. It is not seen where in the rejection the Examiner provided any facts in Tobyn to indicate that simethicone, a viscous oil-like substance, could be adsorbed onto silicified microcrystalline cellulose, much less any facts indicating that silicified microcrystalline cellulose would have the same improved properties when formulated with simethicone. Thus, the rejection is not supported by fact and must be withdrawn for this reason alone.

Further, the Examiner has not provided any facts to support the proposition that using siMCC in Kitsusho's formulation would overcome the problem acknowledged by Kitsusho, e.g., not exceeding 25% simethicone in the formulation. It is not seen where there are any facts in the rejection to suggest any expectation of success for increasing the

amount of simethicone in a formulation using an additional adsorbent, e.g., siMCC. Because it appears that the rejection is based upon possibilities or probabilities, it is improper and should be withdrawn.

Finally, Stevens does not appear to close the gaps in the Examiner's rejection. The sole example in Stevens relied on by the Examiner provides factual evidence that the ratio of simethicone to adsorbent (dibasic calcium phosphate + microcrystalline cellulose + colloidal silicon dioxide) is 125:667, which is 1: 0.18. It is submitted that a ratio of about 0.19 does not fall within the claimed ratio of at least about 0.45. For this additional reason, the rejection is improper and should be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections, and allowance of the claims is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

Respectfully submitted,

By: _____
Timothy E. Tracy
Reg. No. 39,401

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-6586
Dated: January 17, 2005